Application No.: 10/658,298 Amdt dated: January 5, 2005 Reply to OA dated: October 5, 2004

PATENT APPLICATION

## **Amendments to the Claims:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

Claim 1. (original): A compound of formula

$$R^3$$
 $N$ 
 $R^4$ 
 $N$ 
 $R^2$ 
 $R^4$ 
 $N$ 
 $R^2$ 
 $R^4$ 
 $N$ 
 $R^2$ 
 $R^2$ 

or a pharmaceutically acceptable salt thereof, wherein

 $R^1$  is H or  $C_{1-8}$ alkyl;

R<sup>2</sup> is C<sub>1-8</sub>alkyl, phenyl, benzyl, R<sup>c</sup>, R<sup>f</sup>, C<sub>1-4</sub>alkylR<sup>c</sup>, C<sub>1-4</sub>alkylR<sup>f</sup> or R<sup>g</sup>;

 $R^3$  is phenyl, naphthyl, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1-4 heteroatoms selected from N, O and S, wherein no more than 2 of the heteroatoms are O or S, and the heterocycle is substituted by 0, 1 or 2 oxo groups and is optionally fused with a benzo group, any of which are substituted by 0, 1, 2 or 3 substituents selected from  $C_{1-8}$ alkyl,  $C_{1-4}$ haloalkyl, halo, cyano, nitro,  $-C(=O)R^b$ ,  $-C(=O)OR^b$ ,  $-C(=O)NR^aR^a$ ,  $-C(=NR^a)NR^aR^a$ ,  $-OR^a$ ,  $-OC(=O)R^b$ ,  $-OC(=O)NR^aR^a$ ,  $-OC(=O)N(R^a)S(=O)_2R^b$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-S(=O)_2N(R^a)C(=O)R^b$ ,  $-S(=O)_2N(R^a)C(=O)R^b$ ,  $-S(=O)_2N(R^a)C(=O)R^aR^a$ ,  $-N(R^a)C(=O)R^aR^a$ ,  $-N(R^a)C(=O)R^a$ 

 $R^4$  is phenyl, naphthyl, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1-4 heteroatoms selected from N, O and S, wherein no more than 2 of the heteroatoms are O or S, and the heterocycle is substituted by 0, 1 or 2 oxo groups and is optionally fused with a benzo group, any of which are substituted by 0, 1, 2 or 3 substituents selected from  $C_{1-8}$ alkyl,  $C_{1-4}$ haloalkyl, halo, cyano, nitro,  $-C(=O)R^b$ ,  $-C(=O)OR^b$ ,  $-C(=O)NR^aR^a$ ,  $-C(=NR^a)NR^aR^a$ ,  $-OR^a$ ,  $-OC(=O)R^b$ ,  $-OC(=O)NR^aR^a$ ,  $-OC(=O)N(R^a)S(=O)_2R^b$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-OC_{2-6}$ alkyl $NR^a$ ,  $-OC_{2-6}$ alkyl

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 $-N(R^a)C(=NR^a)NR^aR^a, -N(R^a)S(=O)_2R^b, -N(R^a)S(=O)_2NR^aR^a, -NR^aC_{2-6}alkylNR^aR^a \ and -NR^aC_{2-6}alkylOR^a;$ 

R<sup>a</sup> is independently at each instance H or R<sup>b</sup>;

R<sup>b</sup> is independently at each instance C<sub>1-8</sub>alkyl, phenyl or benzyl;

R<sup>c</sup> is independently at each instance a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups;

 $R^{d} \text{ is independently at each instance $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^{b}$, $-C(=O)NR^{a}R^{a}$, $-C(=NR^{a})NR^{a}R^{a}$, $-OR^{a}$, $-OC(=O)R^{b}$, $-OC(=O)NR^{a}R^{a}$, $-OC(=O)N(R^{a})S(=O)_{2}R^{b}$, $-OC_{2-6}alkylNR^{a}R^{a}$, $-OC_{2-6}alkylOR^{a}$, $-SR^{a}$, $-S(=O)R^{b}$, $-S(=O)_{2}R^{b}$, $-S(=O)_{2}NR^{a}R^{a}$, $-S(=O)_{2}N(R^{a})C(=O)R^{b}$, $-S(=O)_{2}N(R^{a})C(=O)NR^{a}R^{a}$, $-NR^{a}R^{a}$, $-N(R^{a})C(=O)R^{b}$, $-N(R^{a})C(=O)NR^{a}R^{a}$, $-N(R^{a})C(=O)R^{b}$, $-N(R^{a})C(=O)R^{b}$, $-N(R^{a})C(=O)R^{a}R^{a}$, $-N(R^{a})C(=O)R^{a}R^{a}R^{a}$, $-N(R^{a})C(=O)R^{a}R^{a}R^{a}$, $-N(R^{a})C(=O)R^{a}R^{a}R^{a}$, $-N(R^{a})C(=O)R^{a}R^{a}R^{a}$, $-N(R^{a})C(=O)R^{$ 

 $R^e$  is independently at each instance  $C_{1-6}$ alkyl substituted by 1, 2 or 3 substituents independently selected from  $R^d$ ;

 $R^{f}$  is independently at each instance  $R^{c}$  substituted by 1, 2 or 3 substituents independently selected from  $R^{d}$ ; and

 $R^g$  is independently at each instance  $R^b$  substituted by 1, 2 or 3 substituents independently selected from  $R^c$ ,  $R^f$  and  $R^d$ .

- Claim 2. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>1</sup> is H.
- Claim 3. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein  $R^1$  is  $C_{1.8}$ alkyl.
- Claim 4. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>2</sup> is R<sup>c</sup>, R<sup>f</sup>, C<sub>1-4</sub>alkylR<sup>c</sup>, C<sub>1-4</sub>alkylR<sup>f</sup> or R<sup>g</sup>.

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Claim 5. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein  $R^2$  is  $C_{1-8}$ alkyl, phenyl or benzyl.

Claim 6. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein  $R^3$  is phenyl or naphthyl both of which are substituted by 0, 1, 2 or 3 substituents selected from  $C_{1-8}$ alkyl,  $C_{1-4}$ haloalkyl, halo, cyano, nitro,  $-C(=O)R^b$ ,  $-C(=O)OR^b$ ,  $-C(=O)NR^aR^a$ ,  $-C(=NR^a)NR^aR^a$ ,  $-OR^a$ ,  $-OC(=O)R^b$ ,  $-OC(=O)NR^aR^a$ ,  $-OC(=O)N(R^a)S(=O)_2R^b$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-S(=O)_2N(R^a)C(=O)R^b$ ,  $-S(=O)_2N(R^a)C(=O)NR^aR^a$ ,  $-NR^aR^a$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^a$ ,  $-N(R^a)C(=O)R$ 

Claim 7. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein  $R^3$  is unsubstituted naphthyl or phenyl substituted by 1, 2 or 3 substituents selected from  $C_{1-8}$ alkyl,  $C_{1-4}$ haloalkyl, halo, cyano, nitro,  $-C(=O)R^b$ ,  $-C(=O)OR^b$ ,  $-C(=O)NR^aR^a$ ,  $-C(=NR^a)NR^aR^a$ ,  $-OR^a$ ,  $-OC(=O)R^b$ ,  $-OC(=O)NR^aR^a$ ,  $-OC(=O)N(R^a)S(=O)_2R^b$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-S(=O)_2N(R^a)$ ,  $-S(=O)_2N(R^a)$ ,  $-S(=O)_2N(R^a)$ ,  $-S(=O)_2N(R^a)$ ,  $-S(=O)_2N(R^a)$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^a$ ,

Claim 8. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>3</sup> is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1-4 heteroatoms selected from N, O and S, wherein no more than 2 of the heteroatoms are O or S, and the heterocycle is substituted by 0, 1 or 2 oxo groups and is optionally fused with a benzo group, any of which are substituted by 0, 1, 2 or 3 C<sub>1-8</sub>alkyl, C<sub>1-4</sub>haloalkyl, halo, cyano, nitro, -C(=O)R<sup>b</sup>, -C(=O)OR<sup>b</sup>, -C(=O)NR<sup>a</sup>R<sup>a</sup>, -C(=NR<sup>a</sup>)NR<sup>a</sup>R<sup>a</sup>, -OR<sup>a</sup>, -OC(=O)R<sup>b</sup>, -OC(=O)NR<sup>a</sup>R<sup>a</sup>, -OC(=O)N(R<sup>a</sup>)S(=O)<sub>2</sub>R<sup>b</sup>, -OC<sub>2-6</sub>alkylNR<sup>a</sup>R<sup>a</sup>, -OC<sub>2-6</sub>alkylOR<sup>a</sup>, -SR<sup>a</sup>, -S(=O)<sub>2</sub>N(R<sup>a</sup>)C(=O)NR<sup>a</sup>R<sup>a</sup>, -S(=O)<sub>2</sub>N(R<sup>a</sup>)C(=O)NR<sup>a</sup>R<sup>a</sup>, -N(R<sup>a</sup>)C(=O)R<sup>b</sup>, -N(R<sup>a</sup>)C(=O)OR<sup>b</sup>, -N(R<sup>a</sup>)C(=O)NR<sup>a</sup>R<sup>a</sup>, -N(R<sup>a</sup>)C(=NR<sup>a</sup>)NR<sup>a</sup>R<sup>a</sup>, -N(R<sup>a</sup>)C(=NR<sup>a</sup>)NR<sup>a</sup>R<sup>a</sup>, -N(R<sup>a</sup>)S(=O)<sub>2</sub>R<sup>b</sup>, -N(R<sup>a</sup>)S(=O)<sub>2</sub>NR<sup>a</sup>R<sup>a</sup>, -NR<sup>a</sup>C<sub>2-6</sub>alkylNR<sup>a</sup>R<sup>a</sup> or -NR<sup>a</sup>C<sub>2-6</sub>alkylOR<sup>a</sup>.

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Claim 9. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein R<sup>4</sup> is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1-4 heteroatoms selected from N, O and S, wherein no more than 2 of the heteroatoms are O or S, and the heterocycle is substituted by 0, 1 or 2 oxo groups and is optionally fused with a benzo group, any of which are substituted by 0, 1, 2 or 3 substituents selected from C<sub>1-8</sub>alkyl, C<sub>1</sub>.

4haloalkyl, halo, cyano, nitro, -C(=O)R<sup>b</sup>, -C(=O)OR<sup>b</sup>, -C(=O)NR<sup>a</sup>R<sup>a</sup>, -C(=NR<sup>a</sup>)NR<sup>a</sup>R<sup>a</sup>, -OR<sup>a</sup>, -OC(=O)R<sup>b</sup>, -OC(=O)NR<sup>a</sup>R<sup>a</sup>, -OC(=O)N(R<sup>a</sup>)S(=O)<sub>2</sub>R<sup>b</sup>, -OC<sub>2-6</sub>alkylNR<sup>a</sup>R<sup>a</sup>, -OC<sub>2-6</sub>alkylOR<sup>a</sup>, -SR<sup>a</sup>, -S(=O)<sub>2</sub>N(R<sup>a</sup>)C(=O)R<sup>b</sup>, -S(=O)<sub>2</sub>N(R<sup>a</sup>)C(=O)OR<sup>b</sup>, -S(=O)<sub>2</sub>N(R<sup>a</sup>)C(=O)OR<sup>b</sup>, -N(R<sup>a</sup>)C(=O)OR<sup>b</sup>, -N(R<sup>a</sup>)C(=O)NR<sup>a</sup>R<sup>a</sup>, -N(R<sup>a</sup>)C(=O)NR<sup>a</sup>R<sup>a</sup>, -N(R<sup>a</sup>)C(=O)R<sup>b</sup>, -N(R<sup>a</sup>)C(=O)NR<sup>a</sup>R<sup>a</sup>, -N(R<sup>a</sup>)C(=O)R<sup>a</sup>R<sup>a</sup>, -N(R<sup>a</sup>)C(=O)R<sup>a</sup>

Claim 10. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein  $R^4$  is phenyl or naphthyl, both of which are substituted by 0, 1, 2 or 3 substituents selected from  $C_{1-8}$ alkyl,  $C_{1-4}$ haloalkyl, halo, cyano, nitro,  $-C(=O)R^b$ ,  $-C(=O)OR^b$ ,  $-C(=O)NR^aR^a$ ,  $-C(=NR^a)NR^aR^a$ ,  $-OR^a$ ,  $-OC(=O)R^b$ ,  $-OC(=O)NR^aR^a$ ,  $-OC(=O)N(R^a)S(=O)_2R^b$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-S(=O)_2N(R^a)C(=O)R^b$ ,  $-S(=O)_2N(R^a)C(=O)NR^aR^a$ ,  $-NR^aR^a$ ,  $-N(R^a)C(=O)R^b$ ,  $-S(=O)_2N(R^a)C(=O)NR^aR^a$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)NR^aR^a$ ,  $-N(R^a)C(=NR^a)NR^aR^a$ ,  $-N(R^a)S(=O)_2NR^aR^a$ ,  $-N(R^a)S(=O)_2NR^a$ 

Claim 11. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein  $R^4$  is pyridine or pyrimidine, both of which are substituted by 0, 1, 2 or 3 substituents selected from  $C_{1-8}$ alkyl,  $C_{1-4}$ haloalkyl, halo, cyano, nitro,  $-C(=O)R^b$ ,  $-C(=O)OR^b$ ,  $-C(=O)NR^aR^a$ ,  $-C(=NR^a)NR^aR^a$ ,  $-OR^a$ ,  $-OC(=O)R^b$ ,  $-OC(=O)NR^aR^a$ ,  $-OC(=O)N(R^a)S(=O)_2R^b$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-OC_{2-6}$ alkyl $NR^aR^a$ ,  $-S(=O)_2N(R^a)C(=O)R^b$ ,  $-S(=O)_2N(R^a)C(=O)NR^aR^a$ ,  $-NR^aR^a$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^b$ ,  $-N(R^a)C(=O)R^aR^a$ ,  $-N(R^a)C(=O)R^a$ 

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Claim 12. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, provided that R<sup>4</sup> is not pyridine or phenyl.

Claim 13. (original): The compound of Claim 1 or a pharmaceutically acceptable salt thereof, wherein the compound is:

4-(4-chloro-phenyl)-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(4-chloro-phenyl)-1-piperidin-4-yl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(4-chloro-phenyl)-1-piperidin-3-yl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(4-chloro-phenyl)-1-piperidin-4-ylmethyl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(4-chloro-phenyl)-1-methyl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(3, 4-dichlorophenyl)-1-piperidin-4-yl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(4-chlorophenyl)-1-(1-methyl-piperidin-4-yl)-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(4-chlorophenyl)-1-(1-methyl-piperidin-3-yl)-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(4-chlorophenyl)-1-(1-isopropyl-piperidin-4-yl)-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-[4-(4-chlorophenyl)-3-methoxy-5-pyridin-4-yl-pyrazol-1-yl]-piperidine;

4-(3,4-dichloro-phenyl)-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(3,4-dichloro-phenyl)-1-isopropyl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(3,4-dichloro-phenyl)-1-isopropyl-2-methyl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

4-(3,4-dichloro-phenyl)-2-methyl-5-pyridin-4-yl-1-pyridin-3-ylmethyl-1,2-dihydro-pyrazol-3-one;

1-cyclohexylmethyl-4-(3,4-dichloro-phenyl)-2-methyl-5-pyridin-4-yl-1,2-dihydro-pyrazol-3-one;

1-(4-aminocyclohexyl)-4-(4-chlorophenyl)-5-pyridin-4-yl-1,2-dihydropyrazol-3-one;

1-(4-aminocyclohexyl)-4-napthalen-2-yl-5-pyridin-4-yl-1,2-dihydropyrazol-3-one; or

4-naphthalen-2-yl-1-(3-phenylpropyl)-5-pyridin-4-1,2-dihydropyrazol-3-one.

Claim 14. (original): A pharmaceutical composition comprising a compound according to Claim 1 and a pharmaceutically acceptable carrier or diluent.

Claims 15-22 (cancelled)

Claim 23. (original): A method of making a compound according to Claim 1, comprising the steps of:

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reacting  $R^3$ -CO<sub>2</sub>H with  $R^4$ -C(=O)H in the presence of trialkylamine and acetic anhydride; protecting the resulting acid with a protecting group; and reacting the protected acid with hydrazine to form